

1

SEQUENCE LISTING

<110> Egelrud, Torbjorn
Hansson, Lennart

<120> SCCE modified transgenic mammals and
their use as models of human diseases

<130> P26024US02

<150> US 60/267,422

<151> 2001-02-09

<150> PA 2001 00218

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986

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3

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ggatggagag	aggaaggaag	aaggagggag	ggagggagag	acaggccaac	ttcatcagcg	9360
tgggaagggg	tgtgaaagtg	tttctgagca	tctcacgagt	gacaagttag	gagggaggct	9420

6

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ggcgggttttc agaggggattg ggatgacagt agacaggaca caggggtccc acaggggtct 9480
gccagaagta agcaaacagt gccggaggaa gatggtggca cctgctcccc aagaaggag 9540
ggaaaggaac ctcggaagc gggtaggatg agggaggagt cctctgtgac tcagagcctg 9600
gccacagccc cagccatcta acatcaaaga tcctctgtgt ggtcacacct cagacgctgc 9660
tgaccgagga gccactccag cccaggacac gccctcctac ctgtttcttc tgtttttctc 9720
ccagaattc 9729

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<210> 4
 <211> 23
 <212> PRT
 <213> Bos taurus

<400> 4
 Ala Gly Ile Pro Asn Ser Arg Thr Asn Ala Cys Asn Gly Asp Ser Gly
 1 5 10 15
 Gly Pro Leu Met Cys Lys Gly
 20

<210> 5
 <211> 23
 <212> PRT
 <213> Sus scrofa

<400> 5
 Ala Gly Ile Pro Asn Ser Lys Thr Asn Ala Cys Asn Gly Asp Ser Gly
 1 5 10 15
 Gly Pro Leu Val Cys Lys Gly
 20

<210> 6
 <211> 23
 <212> PRT
 <213> Homo sapiens

<400> 6
 Ala Gly Ile Pro Asp Ser Lys Lys Asn Ala Cys Asn Gly Asp Ser Gly
 1 5 10 15
 Gly Pro Leu Val Cys Arg Gly
 20

<210> 7
 <211> 23
 <212> PRT
 <213> Rattus norvegicus

<400> 7
 Ala Gly Ile Pro Asp Ser Lys Thr Asn Thr Cys Asn Gly Asp Ser Gly
 1 5 10 15
 Gly Pro Leu Val Cys Asn Asp
 20

<210> 8
 <211> 23
 <212> PRT
 <213> Mus musculus

7

<400> 8

Ala Gly Ile Pro Asp Ser Lys Thr Asn Thr Cys Asn Gly Asp Ser Gly
1 5 10 15
Gly Pro Leu Val Cys Asn Asp
20

<210> 9

<211> 38

<212> PRT

<213> Bos taurus

<400> 9

Gln Glu Asp Gln Gly Asn Lys Ser Gly Glu Lys Ile Ile Asp Gly Val
1 5 10 15
Pro Cys Pro Arg Gly Ser Gln Pro Trp Gln Val Ala Leu Leu Lys Gly
20 25 30
Ser Gln Leu His Cys Gly
35

<210> 10

<211> 37

<212> PRT

<213> Sus scrofa

<400> 10

Gln Glu Gly Gln Asp Lys Ser Gly Glu Lys Ile Ile Asp Gly Val Pro
1 5 10 15
Cys Pro Gly Gly Ser Arg Pro Trp Gln Val Ala Leu Leu Lys Gly Asn
20 25 30
Gln L u His Cys Gly
35

<210> 11

<211> 34

<212> PRT

<213> Homo sapiens

<400> 11

Glu Glu Ala Gln Gly Asp Lys Ile Ile Asp Gly Ala Pro Cys Ala Arg
1 5 10 15
Gly Ser His Pro Trp Gln Val Ala Leu Leu Ser Gly Asn Gln Leu His
20 25 30
Cys Gly

<210> 12

<211> 31

<212> PRT

<213> Rattus norvegicus

<400> 12

Gln Gly Glu Arg Ile Ile Asp Gly Tyr Lys Cys Lys Glu Gly Ser His
1 5 10 15
Pro Trp Gln Val Ala Leu Leu Lys Gly Asp Gln Leu His Cys Gly
20 25 30

8

<210> 13
<211> 31
<212> PRT
<213> Mus musculus

<400> 13
Gln Gly Glu Arg Ile Ile Asp Gly Ile Lys Cys Lys Glu Gly Ser His
1 5 10 15
Pro Trp Gln Val Ala Leu Leu Lys Gly Asn Gln Leu His Cys Gly
20 25 30

<210> 14
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Consensus sequence for cleavage site in C-terminal
of SCCE.

<221> VARIANT
<222> 2
<223> Asp = either aspartate (Asp) or glutamate (Glu).

<221> VARIANT
<222> 3
<223> Lys = either lysine (Lys) or arginine (Arg).

<400> 14
Gly Asp Lys Ile Ile Asp Gly
1 5

<210> 15
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> consensus of the substrate specificity pouch.

<221> VARIANT
<222> 1
<223> Thr = any amino acid residue.

<221> VARIANT
<222> 3
<223> Ala = any amino acid residue.

<221> VARIANT
<222> 5
<223> Asn = any amino acid residue.

<400> 15
Thr Asn Ala Cys Asn Gly Asp Ser
1 5

9

<210> 16
<211> 20
<212> DNA
<213> Artificial sequence

<220>
<223> PCR primer SYM3300.

<400> 16
ggtggccctg ctcaaggcca 20

<210> 17
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer SYM3301.

<400> 17
caccatggat gacacagcct gg 22

<210> 18
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer SYM3302.

<400> 18
aataaagaaa cacaaaaccc 20

<210> 19
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer SYM3418.

<400> 19
tgtaatatca ttgtgggc 18

<210> 20
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer SYM4118.

<400> 20
ggatgtgaag ctcatctc 18

<210> 21
<211> 18

10

<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer SYM4121.

<400> 21
tggagtcggg gatgccag

18

<210> 22
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer SYM4720.

<400> 22
gggaggggtgg agagagagtg cagtg

25

<210> 23
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer SYM4899.

<400> 23
agcttaggct gcagccccta c

21

<210> 24
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer hEXON1.

<400> 24
ctcgagggat ctgatgtgat cc

22

<210> 25
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer mEXON1.

<400> 25
ctgggagtga cttggcgtgg ctct

24

<210> 26
<211> 23
<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer specific for human SCCE IE2.

<400> 26

gctctcccat tagtccccag aga

23

<210> 27

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer specific for human SCCE MJ2.

<400> 27

ccacttggtg aacttgacaca cttg

24

<210> 28

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> forward primer covering the position 427 - 444 of the human SCCE cDNA sequence.

<400> 28

gggaaccccc tggaacaa

18

<210> 29

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> reverse primer covering the position 490 - 510 of the human cDNA sequence in exon five.

<400> 29

acatccacgc acatgaggtc a

21

<210> 30

<211> 29

<212> DNA

<213> Artificial Sequence

<220>

<223> The real time amplification probe covering the position 445 - 473 of the human cDNA sequence in exon four.

<400> 30

cctgtactgt ctccggctgg ggcactacc

29

12

<210> 31
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer mS3.

<400> 31
caaggagaaa ggattataga tggct

25

<210> 32
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer 698.

<400> 32
aaggctccgc acccatggca g

21

<210> 33
<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer 696.

<400> 33
tgcaatggtg actcaggggg gccctt

26

<210> 34
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer H2.

<400> 34
gaccagggcg tctacactca agt

23

<210> 35
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer mS4.

<400> 35
gagaccatga aaacccatcg ctaac

25

<210> 36

13

<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer KO 0905.

<400> 36
tgactttctt cacactggac gacagc 26

<210> 37
<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer GR 0905.

<400> 37
cttcacactg gctgatagcc tggccg 26

<210> 38
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer Ngr.

<400> 38
cagggtggcg gaatgacctc atggccct 28

<210> 39
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer RA 1016.

<400> 39
ctactccaca aggacccatg tcaatgac 28

<210> 40
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer nRA 1016.

<400> 40
gctgtgtgct ggcattcccg actctaag 28

<210> 41
<211> 30

14

<212> DNA
<213> Artificial Sequence

<220>
<223> SMART II oligonucleotide.

<400> 41
aagcagtggg aacaacgcag agtacgcggg 30

<210> 42
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> 5'-RACE cDNA synthesis primer.

<221> variation
<222> 27
<223> n = a or g or c or t

<400> 42
ttttttttt ttttttttt tttttvn 27

<210> 43
<211> 45
<212> DNA
<213> Artificial Sequence

<220>
<223> Long universal primer.

<400> 43
ctaatacgac tcactatagg gcaagcagtg gtaacaacgc agagt 45

<210> 44
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Short universal primer.

<400> 44
ctaatacgac tcactatagg gcc 23

<210> 45
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Nested universal primer.

<400> 45
aagcagtggg aacaacgcag agt 23

<210> 46
<211> 243
<212> PRT

15

<213> Artificial Sequence

<220>

<223> Deduced amino acid sequence from the C-terminal
part of SCCE from cow.

<400> 46

```

Met Thr Thr Pro Leu Val Ile Leu Leu Leu Thr Phe Ala Leu Gly Ser
 1           5           10           15
Val Ala Gln Glu Asp Gln Gly Asn Lys Ser Gly Glu Lys Ile Ile Asp
          20           25           30
Gly Val Pro Cys Pro Arg Gly Ser Gln Pro Trp Gln Val Ala Leu Leu
      35           40           45
Lys Gly Ser Gln Leu His Cys Gly Gly Val Leu Leu Asn Glu Gln Trp
      50           55           60
Val Leu Thr Ala Ala His Cys Met Asn Glu Tyr Asn Val His Met Gly
      65           70           75           80
Ser Val Arg Leu Val Gly Gly Gln Lys Ile Lys Ala Thr Arg Ser Phe
          85           90           95
Arg His Pro Gly Tyr Ser Thr Gln Thr His Ala Asn Asp Leu Met Leu
          100          105          110
Val Lys Leu Asn Gly Arg Ala Lys Leu Ser Ser Ser Val Lys Lys Val
          115          120          125
Asn Leu Pro Ser His Cys Asp Pro Pro Gly Thr Met Cys Thr Val Ser
          130          135          140
Gly Trp Gly Thr Thr Thr Ser Pro Asp Val Thr Phe Pro Gly Gln Leu
          145          150          155          160
Met Cys Thr Asp Val Lys Leu Ile Ser Pro Gln Asp Cys Arg Lys Val
          165          170          175
Tyr Lys Asp Leu Leu Gly Asp Ser Met Leu Cys Ala Gly Ile Pro Asn
          180          185          190
Ser Arg Thr Asn Ala Cys Asn Gly Asp Ser Gly Gly Pro Leu Met Cys
          195          200          205
Lys Gly Thr Leu Gln Gly Val Val Ser Trp Gly Ser Phe Pro Cys Gly
          210          215          220
Gln Pro Asn Asp Pro Gly Val Tyr Thr Gln Val Cys Lys Tyr Val Asn
          225          230          235          240
Trp Ile Lys

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<210> 47

<211> 249

<212> PRT

<213> Artificial Sequence

<220>

<223> Deduced amino acid sequence from the C-terminal
part of SCCE from pig.

<400> 47

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Met Ala Arg Pro Leu Leu Pro Pro Arg Leu Ile Leu Leu Ser Leu
 1           5           10           15
Ala Leu Gly Ser Ala Ala Gln Glu Gly Gln Asp Lys Ser Gly Glu Lys
          20           25           30
Ile Ile Asp Gly Val Pro Cys Pro Gly Gly Ser Arg Pro Trp Gln Val
          35           40           45
Ala Leu Leu Lys Gly Asn Gln Leu His Cys Gly Gly Val Leu Val Asn
          50           55           60
Gln Gln Trp Val Leu Thr Ala Ala His Cys Met Met Asn Asp Tyr Asn
          65           70           75           80

```

16

Val His Leu Gly Ser Asp Arg Leu Asp Asp Arg Lys Gly Gln Lys Ile
 85 90 95
 Arg Ala Met Arg Ser Phe Arg His Pro Gly Tyr Ser Thr Gln Thr His
 100 105 110
 Val Asn Asp Leu Met Leu Val Lys Leu Ser Arg Pro Ala Arg Leu Ser
 115 120 125
 Ala Ser Val Lys Lys Val Asn Leu Pro Ser Arg Cys Glu Pro Pro Gly
 130 135 140
 Thr Thr Cys Thr Val Ser Gly Trp Gly Thr Thr Thr Ser Pro Asp Val
 145 150 155 160
 Thr Phe Pro Ala Asp Leu Met Cys Thr Asp Val Lys Leu Ile Ser Ser
 165 170 175
 Gln Asp Cys Lys Lys Val Tyr Lys Asp Leu Leu Gly Ser Ser Met Leu
 180 185 190
 Cys Ala Gly Ile Pro Asn Ser Lys Thr Asn Ala Cys Asn Gly Asp Ser
 195 200 205
 Gly Gly Pro Leu Val Cys Lys Gly Thr Leu Gln Gly Leu Val Ser Trp
 210 215 220
 Gly Thr Phe Pro Cys Gly Gln Pro Asn Asp Pro Gly Val Tyr Thr Gln
 225 230 235 240
 Val Cys Lys Tyr Ile Asp Trp Ile Asn
 245

<210> 48

<211> 253

<212> PRT

<213> Artificial Sequence

<220>

<223> Deduced amino acid sequence from the C-terminal
 part of SCCE from homo.

<400> 48

Met Ala Arg Ser Leu Leu Leu Pro Leu Gln Ile Leu Leu Leu Ser Leu
 5 10 15
 Ala Leu Glu Thr Ala Gly Glu Glu Ala Gln Gly Asp Lys Ile Ile Asp
 20 25 30
 Gly Ala Pro Cys Ala Arg Gly Ser His Pro Trp Gln Val Ala Leu Leu
 35 40 45
 Ser Gly Asn Gln Leu His Cys Gly Gly Val Leu Val Asn Glu Arg Trp
 50 55 60
 Val Leu Thr Ala Ala His Cys Lys Met Asn Glu Tyr Thr Val His Leu
 65 70 75 80
 Gly Ser Asp Thr Leu Gly Asp Arg Arg Ala Gln Arg Ile Lys Ala Ser
 85 90 95
 Lys Ser Phe Arg His Pro Gly Tyr Ser Thr Gln Thr His Val Asn Asp
 100 105 110
 Leu Met Leu Val Lys Leu Asn Ser Gln Ala Arg Leu Ser Ser Met Val
 115 120 125
 Lys Lys Val Arg Leu Pro Ser Arg Cys Glu Pro Pro Gly Thr Thr Cys
 130 135 140
 Thr Val Ser Gly Trp Gly Thr Thr Thr Ser Pro Asp Val Thr Phe Pro
 145 150 155 160
 Ser Asp Leu Met Cys Val Asp Val Lys Leu Ile Ser Pro Gln Asp Cys
 165 170 175
 Thr Lys Val Tyr Lys Asp Leu Leu Glu Asn Ser Met Leu Cys Ala Gly
 180 185 190
 Ile Pro Asp Ser Lys Lys Asn Ala Cys Asn Gly Asp Ser Gly Gly Pro
 195 200 205
 Leu Val Cys Arg Gly Thr Leu Gln Gly Leu Val Ser Trp Gly Thr Phe

17

210		215		220
Pro Cys Gly Gln Pro Asn Asp Pro Gly Val Tyr Thr Gln Val Cys Lys				
225		230		235
Phe Thr Lys Trp Ile Asn Asp Thr Met Lys Lys His Arg				240
	245		250	

<210> 49

<211> 226

<212> PRT

<213> Artificial Sequence

<220>

<223> Deduced amino acid sequence from the C-terminal part of SCCE from rat.

<400> 49

Met Gly Val Trp Leu Leu Ser Leu Leu Thr Val Leu Leu Ser Leu Ala				
1	5	10	15	
Leu Glu Thr Ala Gly Gln Gly Glu Arg Ile Ile Asp Gly Tyr Lys Cys				
	20	25	30	
Lys Glu Gly Ser His Pro Trp Gln Val Ala Leu Leu Lys Gly Asp Gln				
	35	40	45	
Leu His Cys Gly Gly Val Leu Val Gly Glu Ser Trp Val Leu Thr Ala				
	50	55	60	
Ala His Cys Lys Met Gly Gln Tyr Thr Val His Leu Gly Ser Asp Lys				
	65	70	75	80
Ile Glu Asp Gln Ser Ala Gln Arg Ile Lys Ala Ser Arg Ser Phe Arg				
	85	90	95	
His Pro Gly Tyr Ser Thr Arg Thr His Val Asn Asp Ile Met Leu Val				
	100	105	110	
Lys Met Asp Lys Pro Val Lys Met Ser Asp Lys Val Gln Lys Val Lys				
	115	120	125	
Leu Pro Asp His Cys Glu Pro Pro Gly Thr Leu Cys Thr Val Ser Gly				
	130	135	140	
Trp Gly Thr Thr Thr Ser Pro Asp Val Thr Phe Pro Ser Asp Leu Met				
	145	150	155	160
Cys Ser Asp Val Lys Leu Ile Ser Ser Gln Glu Cys Lys Lys Val Tyr				
	165	170	175	
Lys Asp Leu Leu Gly Lys Thr Met Leu Cys Ala Gly Ile Pro Asp Ser				
	180	185	190	
Lys Thr Asn Thr Cys Asn Gly Asp Ser Gly Gly Pro Leu Val Cys Asn				
	195	200	205	
Asp Thr Leu Gln Gly Leu Val Ser Trp Gly Thr Tyr Pro Cys Gly Gln				
	210	215	220	
Pro Asn				
225				

<210> 50

<211> 249

<212> PRT

<213> Artificial Sequence

<220>

<223> Deduced amino acid sequence from the C-terminal part of SCCE from mouse.

<400> 50

Met Gly Val Trp Leu Leu Ser Leu Ile Thr Val Leu Leu Ser Leu Ala			
1	5	10	15

18

Leu Glu Thr Ala Gly Gln Gly Glu Arg Ile Ile Asp Gly Ile Lys Cys
20 25 30
Lys Glu Gly Ser His Pro Trp Gln Val Ala Leu Leu Lys Gly Asn Gln
35 40 45
Leu His Cys Gly Gly Val Leu Val Asp Lys Tyr Trp Val Leu Thr Ala
50 55 60
Ala His Cys Lys Met Gly Gln Tyr Gln Val Gln Leu Gly Ser Asp Lys
65 70 75 80
Ile Gly Asp Gln Ser Ala Gln Lys Ile Lys Ala Thr Lys Ser Phe Arg
85 90 95
His Pro Gly Tyr Ser Thr Lys Thr His Val Asn Asp Ile Met Leu Val
100 105 110
Arg Leu Asp Glu Pro Val Lys Met Ser Ser Lys Val Glu Ala Val Gln
115 120 125
Leu Pro Glu His Cys Glu Pro Pro Gly Thr Ser Cys Thr Val Ser Gly
130 135 140
Trp Gly Thr Thr Thr Ser Pro Asp Val Thr Phe Pro Ser Asp Leu Met
145 150 155 160
Cys Ser Asp Val Lys Leu Ile Ser Ser Arg Glu Cys Lys Lys Val Tyr
165 170 175
Lys Asp Leu Leu Gly Lys Thr Met Leu Cys Ala Gly Ile Pro Asp Ser
180 185 190
Lys Thr Asn Thr Cys Asn Gly Asp Ser Gly Gly Pro Leu Val Cys Asn
195 200 205
Asp Thr Leu Gln Gly Leu Ala Ser Arg Gly Thr Tyr Pro Cys Gly Gln
210 215 220
Pro Asn Asp Pro Gly Val Tyr Thr Gln Val Cys Lys Tyr Lys Arg Trp
225 230 235 240
Val Met Glu Thr Met Lys Thr His Arg
245